

~~(iv) determining each mass label by mass spectrometry to relate the feature of each fragment to the length of the fragment in order to characterize said DNA.~~

2. (Amended) A method according to claim 1, which further comprises the following steps before step (i):

(a) providing at least one DNA single-stranded template primed with a primer; and

(b) generating the population of fragments of said DNA from the at least one template, wherein the population comprises at least one series of DNA fragments, the or each series containing all possible lengths of a second strand of DNA complementary to the or each template;

wherein the feature of each fragment determined by each mass label relates to a nucleotide or nucleotide sequence at one end of each fragment, so that each nucleotide is related to a position in the template associated with the mass label so as to deduce the sequence of the or each template.

3. (Amended) A method according to claim 2, wherein the series of DNA fragments is provided by contacting the template in the presence of DNA polymerase with a mixture of nucleotides for hybridising to the template for forming a second strand of DNA complementary to the template, wherein the mixture further comprises a set of four probes containing all four nucleotides for hybridising to the template in which the nucleotide of each probe comprises a modified nucleotide which is capable of polymerising to the second strand of DNA but blocked to prevent further polymerisation thereto and which is cleavably

attached to the mass label, which mass label is uniquely resolvable in mass spectrometry for identifying the modified nucleotide, and wherein each fragment is terminated with one of the probes.

4. (Amended) A method according to claim 2, wherein the at least one template is a plurality of templates and the series of DNA fragments is provided by contacting each template in a separate reaction vessel in the presence of DNA polymerase with a mixture of nucleotides for hybridising to the template for forming a second strand of DNA complementary to the template, wherein the mixture further comprises a set of four probes containing all four nucleotides for hybridising to the template in which the nucleotide of each probe comprises a modified nucleotide which is capable of polymerising to the second strand of DNA but blocked to prevent further polymerisation thereto and which is cleavably attached to the mass label, which mass label is uniquely resolvable in mass spectrometry for identifying the modified nucleotide, wherein each fragment is terminated with one of the probes, and wherein each set of mass labels from each set of four probes associated with each reaction vessel is different from the other sets of mass labels; and the fragments are pooled before step (ii).

5. (Amended) A method according to claim 2, wherein the at least one template is a plurality of templates and the series of DNA fragments is provided by contacting each template in a separate reaction vessel in the presence of DNA polymerase with a mixture of nucleotides for hybridising to the template for forming a second strand of DNA

complementary to the template, wherein the mixture further comprises a probe containing only one of the four nucleotides for hybridising to the template, the nucleotide of which probe comprises a modified nucleotide which is capable of polymerising to the second strand of DNA but blocked to prevent further polymerisation thereto, wherein each fragment is terminated with the probe and wherein either the primer or the modified nucleotide of the probe is cleavably attached to the mass label, which mass label is associated with the reaction vessel and uniquely resolvable in mass spectrometry from the mass label in the other reaction vessels for identifying the modified nucleotide used in the reaction vessel and the fragments are pooled before step (ii).

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6. (Amended) A method according to claim 2, wherein the at least one template is a plurality of templates and the series of DNA fragments is provided by contacting the plurality of templates in each of four separate reaction vessels in the presence of DNA polymerase with a mixture of nucleotides for hybridising to the template for forming a second strand of DNA complementary to the template, wherein the mixture further comprises a probe containing in each of the reaction vessels only one of the four nucleotides for hybridising to the template, the nucleotide of which probe comprises a modified nucleotide which is capable of polymerising to the second strand of DNA but blocked to prevent further polymerisation thereto, wherein each fragment is terminated with the probe and wherein the primer is cleavably attached to the mass label, which mass label is associated with the primer and uniquely resolvable in mass spectrometry from the mass

labels associated with the other primers used in the reaction zone; and wherein each nucleotide from its corresponding reaction vessel is related to its position in the template.

7. (Amended) A method according to claim 2, wherein the at least one template is four sets of DNA single-stranded templates, each set comprising an identical plurality of DNA single-stranded templates and the series of DNA fragments is provided by contacting each set in a separate reaction vessel in the presence of DNA polymerase with a mixture of nucleotides for hybridising to the templates for forming a second strand of DNA complementary thereto, wherein the mixture further comprises a probe containing in each of the reaction vessels only one of the four nucleotides for hybridising to the template, the nucleotide of which probe comprises a modified nucleotide which is capable of polymerising to the second strand of DNA but blocked to prevent further polymerization thereto, wherein each fragment is terminated with the probe and wherein each of the templates of the four sets is primed with a primer to which the mass label is cleavably attached, which mass label which uniquely resolvable in mass spectrometry from the mass labels corresponding to the other templates and which is relatable to its respective template and its respective reaction vessel wherein the fragments are pooled before step (ii), and each nucleotide from its corresponding reaction zone is related to its position in the template.

8. (Amended) A method according to claim 2, wherein the at least one template is a plurality of templates and the series of DNA fragments is provided by contacting each set

of templates in a separate reaction vessel in the presence of DNA polymerase with a mixture of nucleotides for hybridising to the templates for forming a second strand of DNA complementary thereto, wherein the mixture further comprises a set of four probes containing all four nucleotides for hybridising to the template in which the nucleotide of each probe comprises a modified nucleotide which is capable of polymerising to the second strand of DNA but blocked to prevent further polymerisation thereto and which is cleavable attached to the mass label, which mass label is uniquely resolvable in mass spectrometry for identifying the modified nucleotide, wherein each fragment is terminated with one of the probes, and wherein each set of mass labels from each set of four probes associated with each reaction vessel is different from the other sets of mass labels and, before step (ii), the fragments are pooled and the pooled fragments are sorted according to a sub-sequence having a common length of 3 to 5 bases adjacent to the primer to form an array of groups of sorted fragments, wherein each group is spatially separated from the other groups.

9. (Amended) A method according to claim 2, wherein the series of DNA fragments is provided by

(i) contacting the template in the presence of DNA polymerase with a mixture of nucleotides for hybridising to the template for forming a second strand of DNA complementary to the template, wherein the mixture further comprises a set of four probes containing all four nucleotides for hybridising to the templates in which the nucleotide of each probe comprises a modified nucleotide which is capable of polymerising to the second strand of DNA but reversibly blocked to prevent further polymerisation thereto, wherein

the step of contacting forms a series of templates containing all possible lengths of the second strand of DNA, each second strand terminated with one of the probes;

(ii) removing unincorporated nucleotides;

(iii) unblocking the modified nucleotides; and

(iv) contacting the series of templates with an array of oligonucleotide probes,

wherein each oligonucleotide probe has a nucleotide sequence of common length 2 to 6, all combinations of nucleotide sequences are present in the array, and wherein each probe is cleavably attached to the mass label, which mass label is uniquely resolvable in mass spectrometry for identifying the nucleotide sequence.

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10. (Amended) A method according to claim 2, wherein the at least one template is a plurality of primed DNA single-stranded templates, each at a unique concentration, and the series of DNA fragments is provided by

(i) contacting the templates in the presence of DNA polymerase with a mixture of nucleotides for hybridising to the template for forming a second strand of DNA complementary to the templates, wherein the mixture further comprises a set of four probes containing all four nucleotides for hybridising to the templates in which the nucleotide of each probe comprises a modified nucleotide which is capable of polymerising to the second strand of DNA but reversibly blocked to prevent further polymerisation thereto, wherein the step of contacting forms a series of templates containing all possible lengths of the second strand of DNA, each second strand terminated with one of the probes;

(ii) removing unincorporated nucleotides;

(iii) unblocking the modified nucleotides; and

(iv) contacting the series of templates with an array of oligonucleotide probes, wherein each oligonucleotide probe has a nucleotide sequence of common length 2 to 6, all combinations of nucleotide sequences are present in the array, and wherein each probe is cleavably attached to the mass label, which mass label is uniquely resolvable in mass spectrometry for identifying the nucleotide sequence.

11. (Amended) A method according to claim 2, wherein the series of DNA fragments is provided by contacting the template in the presence of DNA ligase with a mixture of oligonucleotides for hybridising to the template for forming a second strand of DNA complementary to the template, the oligonucleotides each having a common length in the range 2 to 6, wherein the mixture further comprises a set of probes containing all possible oligonucleotides of the common length L for hybridising to the templates in which the oligonucleotide of each probe comprises a modified oligonucleotide which is capable of ligating to the second strand of DNA but blocked to prevent further ligation thereto and which is cleavable attached to the mass label, which mass label is uniquely resolvable in mass spectrometry for identifying the modified oligonucleotide, and the series of fragments contains all possible lengths of the second strand of DNA of integer multiples of L in which each fragment is terminated with one of the probes.

12. (Amended) A method according to claim 2, wherein the at least one template is a plurality of primed DNA single-stranded templates, each at a unique concentration, and

the series of DNA fragments is provided by contacting the templates in the presence of DNA ligase with a mixture of oligonucleotides for hybridising to the templates for forming a second strand of DNA complementary to the templates, the oligonucleotides each having a common length in the range 2 to 6, wherein the mixture further comprises a set of probes containing all possible oligonucleotides of the common length L for hybridising to the templates in which the oligonucleotide of each probe comprises a modified oligonucleotide which is capable of ligating to the second strand of DNA but blocked to prevent further ligation thereto and which is cleavably attached to the mass label, which mass label is uniquely resolvable in mass spectrometry for identifying the modified oligonucleotide, and the series of fragments contains all possible lengths of the second strand of DNA of integer multiples of L in which each fragment is terminated with one of the probes.

13. (Amended Twice) A method according to claim 5, wherein the plurality of single-stranded templates is primed by hybridising to a known sub-sequence common to each of the templates an array of primers each comprising a base sequence containing a common sequence complementary to the known sub-sequence and a variable sequence of common length, in the range of 2 to 6, in which the array contains all possible nucleotide sequences of that common length and the mass label cleavably attached to each primer identifies the variable sequence, which variable sequence identifies the template to be sequenced.

21. (Amended) A method for characterising DNA, which comprises

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- (a) providing a primed DNA single-stranded template;
- (b) contacting the template in the presence of DNA polymerase with a mixture of nucleotides for hybridising to the template for forming a second strand of DNA complementary to the template, wherein the mixture further comprises a set of four probes containing all four nucleotides for hybridising to the templates in which the nucleotide of each probe comprises a modified nucleotide which is capable of polymerising to the second strand of DNA but reversibly blocked to prevent further polymerisation thereto, wherein the step of contacting forms a series of templates containing all possible lengths of the second strand of DNA, each second strand terminated with one of the probes;
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- (c) removing unincorporated nucleotides;
- (d) unblocking the modified nucleotides;
- (e) contacting the series of templates with an array of oligonucleotide probes to form a series of fragments, each oligonucleotide probe having a nucleotide sequence of common length 2 to 6, and all combinations of sequences being present in the array, wherein each probe is cleavably attached to a mass label uniquely resolvable in mass spectrometry for identifying the nucleotide sequence;
- (f) separating the fragments from one another on the basis of their length;
- (g) cleaving each fragment to release its mass label; and
- (h) determining each mass label by mass spectrometry to relate a nucleotide sequence that corresponds to the mass label to a position in the template so as to deduce the sequence of the template in order to characterise the DNA.

22. (Amended) A method for characterising DNA, which comprises
- (a) providing a plurality of primed DNA single-stranded templates, each at a unique concentration;
 - (b) contacting the templates in the presence of DNA polymerase with a mixture of nucleotides for hybridising to the template for forming a second strand of DNA complementary to the templates, wherein the mixture further comprises a set of four probes containing all four nucleotides for hybridising to the templates in which the nucleotide of each probe comprises a modified nucleotide which is capable of polymerising to the second strand of DNA but reversibly blocked to prevent further polymerisation thereto, wherein the step of contacting forms a series of templates containing all possible lengths of the second strand of DNA, each second strand terminated with one of the probes;
 - (c) removing unincorporated nucleotides;
 - (d) unblocking the modified nucleotides;
 - (e) contacting the series of templates with an array of oligonucleotide probes to form a series of fragments, each oligonucleotide probe having a nucleotide sequence of common length 2 to 6, and all combinations of sequences being present in the array, wherein each probe is cleavably attached to a mass label uniquely resolvable in mass spectrometry for identifying the nucleotide sequence;
 - (f) separating the fragments from one another on the basis of their length;
 - (g) cleaving each fragment to release its mass label; and
 - (h) determining the identity and amount of each mass label by mass spectrometry to relate a nucleotide sequence of a probe that corresponds to the mass label to

a position in its respective template so as to deduce the sequence of the template in order to characterise the DNA.

23. (Amended) A method for characterising DNA, which comprises

- (a) providing a primed DNA single-stranded template;
- (b) contacting the template in the presence of DNA ligase with a mixture of oligonucleotides for hybridising to the template for forming a second strand of DNA complementary to the template, the oligonucleotides each having a common length in the range 2 to 6, wherein the mixture further comprises a set of probes containing all possible oligonucleotides of the common length L for hybridising to the templates in which the oligonucleotide of each probe comprises a modified oligonucleotide which is capable of ligating to the second strand of DNA but blocked to prevent further ligation thereto and which is cleavably attached to a corresponding mass label uniquely resolvable in mass spectrometry for identifying the modified oligonucleotide, wherein the step of contacting forms a series of fragments containing all possible lengths of the second strand of DNA of integer multiples of L, each fragment terminated with one of the probes;
- (c) separating the fragments from one another on the basis of their length;
- (d) cleaving each fragment to release its mass label; and
- (e) determining each mass label by mass spectrometry to relate its corresponding oligonucleotide to a position in the template so as to deduce the sequence of the template in order to characterise the DNA.

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24. (Amended) A method for characterising DNA, which comprises

(a) providing a plurality of primed DNA single-stranded templates, each at a unique concentration;

(b) contacting the templates in the presence of DNA ligase with a mixture of oligonucleotides for hybridising to the templates for forming a second strand of DNA complementary to the templates, the oligonucleotides each having a common length in the range 2 to 6, wherein the mixture further comprises a set of probes containing all possible oligonucleotides of the common length L for hybridising to the templates in which the oligonucleotide of each probe comprises a modified oligonucleotide which is capable of ligating to the second strand of DNA but blocked to prevent further ligation thereto and which is cleavably attached to a corresponding mass label uniquely resolvable in mass spectrometry for identifying the modified oligonucleotide, wherein the step of contacting forms a series of fragments containing all possible lengths of the second strand of DNA of integer multiples of L, each fragment terminated with one of the probes;

(c) separating the fragments from one another on the basis of their length;

(d) cleaving each fragment to release its mass label; and

(e) determining the identity and amount of each mass label by mass spectrometry to relate its corresponding oligonucleotide to a position in its respective template so as to deduce the sequence of the template in order to characterise the DNA.

Please cancel claims 25 and 26 without prejudice and replace them with claims 27 and 28.

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27. (New) A method for characterizing DNA, which comprises:

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(a) providing at least one DNA single-stranded template primed with a primer;

(b) generating a population of fragments of said DNA from the at least one template by contacting the at least one template in the presence of DNA polymerase with a mixture of nucleotides for hybridising to the at least one template for forming a second strand of DNA complementary to the at least one template, wherein the mixture further comprises a set of four probes containing all four nucleotides for hybridising to the at least one template in which the nucleotide of each probe comprises a modified nucleotide or oligonucleotide which is capable of polymerising to the second strand of DNA but blocked to prevent further polymerisation thereto, which modified nucleotide or oligonucleotide is cleavably attached to the mass label for identifying the modified nucleotide or oligonucleotide, which mass label is cleavable from the probe in a mass spectrometer and is resolvable by mass spectrometry, and wherein each fragment is terminated with one of the probes, wherein the population comprises at least one series of DNA fragments, the or each series containing all possible lengths of a second strand of DNA complementary to the or each template;

(c) separating the fragments on the basis of their length;

(d) cleaving each fragment in a mass spectrometer to release its mass label; and

(e) determining each mass label by mass spectrometry to relate a terminating modified nucleotide or oligonucleotide of each fragment to the length of the fragment in order to characterize said DNA.

28. (New) A method for characterizing DNA, which comprises: